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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,866	05/04/2001	Duncan McRee	22700-706	8379
32793	7590	04/19/2005	EXAMINER	
SYRRX, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121			BORIN, MICHAEL L	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/848,866

Applicant(s)

MCREE ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-57 is/are pending in the application.
- 4a) Of the above claim(s) 8-12, 15, 17-20, 27-30, 37, 39, 41, 43, 44, 46 and 47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 16, 21-26, 31-36, 38, 40, 42, 45 and 48-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 03/14/2005
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

Amendment filed 01/26/2005 is acknowledged.

Claims 1-57 are pending. Claims 8-12,15,17-20,27-30,37,39, 41,43, 44,46, 47 remain withdrawn from consideration as drawn to non-elected species. Claims 1-7,16,21-26,31-36,38,40,42,45,48-57 are under examination.

Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections constitute the complete set presently being applied to the instant application.

Applicant amended the claims to clarify that the multiple molecular replacement searches are performed using structures of different biomolecules, rather than different structures of the same biomolecule (which was addressed in the art rejections made in the previous Office action). Consequently, the art rejections are withdrawn and the following new rejection is made.

Claim Rejections - 35 USC § 103.

Claims 1-7,16,21-26,31-36,38,40,42,45,48-57 are rejected under 35 U.S.C. 103(a) as obvious over Kissinger et al. (Acta Crystallographica Section D, Biological Crystallography, 1999, D55, 484-491).

The instant claims are drawn to method for identifying a search model to use in molecular replacement for determining a structure of a target biomolecule from crystal data, the method comprising:

employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule where a group of structures of different biomolecules are used as search models for the multiple molecular replacement searches; and

employing computer executable logic to compare solutions from the multiple molecular replacement searches, the comparison producing data from which biomolecule structures in the group can be identified as having superior structural identity with the target biomolecule as compared to the other biomolecule structures in the group.

Kissinger teaches method of automated molecular replacement by evolutionary search, EPMR (*cf.* instant claim 40). The method describes computerized method of molecular replacement wherein the target structure is determined using a search model. A population of initially random molecular-replacement solutions is iteratively optimized with respect to the correlation coefficient between observed and calculated structure factors. The referenced method uses statistical analysis to identify validity of molecular replacement solution. Unlike the instant method, Kissinger reference does not teach use of multiple search models. However, the reference clearly addresses such parallel approach of using multiple search models as one of potential enhancements of EPMR method. Thus, on p. 490, right column, Kissinger discusses that instead of a single search model, a set of structural models that would compete in the evolutionary search process is a useful alternative and is preferable as it will greatly expand the range of applicability of MR.

It would be *prima facie* obvious to substitute single search model method of molecular replacement with using multiple search models and multiple molecular

replacements because Kissinger teaches that using multiple search models will enhance the applicability of the MR method and will enhance the search efficiency. One would expect that the possibility of success in utilizing multiple search models in the method of Kissinger will be at least as effective as the use of single search model.

With respect to claims 53-55, it would be obvious that the selection of different structures should continue until a molecular replacement is produced, and then to use such molecular replacement to identify the structure of the target molecule - the latter being the final objective of any method of molecular replacement.

Further, with respect to dependent claims addressing particular criteria of selecting structures, conducting the method, and comparing the degree of similarity of structures, the reference does not expressly teach these criteria, as it is drawn to use of single model, rather than plurality of models. Absent some teaching to the contrary however, the determination of such criteria is within the skill of the ordinary worker as a part of the process of normal optimization. Applicant's claims are directed to optimization of an "art recognized variables" which is well within the pervue of one of ordinary skill in the art. In re Boesch, 617 F. 2d 272, 205 USPQ 215 (CCPA 1980).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
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